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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,432	12/12/2003	Eric Thwaites	10281.400-US	3883

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EXAMINER	
PETERSEN, CLARK D	

ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
05/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,432	THWAITES, ERIC	
	Examiner	Art Unit	
	Clark D. Petersen	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8 and 12-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 1 March 2007, in which claims 2, 3, 9-11, and 17 were canceled and claim 1 was amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All objections and rejections not repeated in the instant Action have been withdrawn due to Applicant's response to the previous Action.

Double Patenting

Based on Applicants' abandonment of the co-filed application serial no. 10/463939, the rejection of claims 1-8 on the grounds of nonstatutory obviousness-type double patenting is withdrawn.

Claim Rejections - 35 USC § 102

Applicants traverse the rejection of claims 1, 2, 4-6, 8, and 16 in the Office Action mailed 16 November 2006 under 35 USC 102(b) as being anticipated by Bracke et al (US 4,517,295). Based on Applicants' amendment, this rejection is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-8 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weigel et al (International Patent Publication #WO99/23227, published 14 May, 1999) in view of Kanani et al (US Patent #3,878,093, issued 15 Apr 1975).

This rejection was originally presented in the Office Action mailed 16 November 2006 and is maintained for reasons of record, and as set forth below.

Weigel et al teach a method of fermenting a microorganism. This microorganism is capable of producing a glycosaminoglycan and secreting it into its medium. In particular it is advantageous, after the glycosaminoglycan has been produced, to sequester the microorganism from its fermentation broth, by a method of flocculating the microorganism (see p. 63, lines 6-23, for example). In particular the microorganism that produces the glycosaminoglycan can be either a eukaryote or a prokaryote (see p. 58, line 27 to p. 59, line 8, for example; see p. 59, line 18 to p. 60, line 8, for example). In particular, the use of *Bacillus subtilis* is a preferred embodiment of a cultured organism for producing the glycosaminoglycan hyaluronic acid (see p. 59, lines 9-17, for example). These hyaluronic acid molecules span a range of sizes, but fall within the range recited in the instant claim 5 (see p. 79, lines 11-23, for example; see Fig. 9, for example).

Weigel et al do not expressly teach addition of a divalent salt as a flocculating agent.

Weigel et al do not expressly teach adjusting the fermentation broth pH.

Weigel et al do not expressly teach heating the fermentation broth to between 30 and 60 °C.

Kanani et al teach that it is possible to separate a microorganism from its fermentation broth by flocculation. This flocculation can be achieved by raising the pH of the fermentation broth to 8 to 11, followed by heating the fermentation broth to a minimum of 50 °C; and changing the pH of the fermentation broth to between 2 and 5 by addition of acid (see col. 1, lines 36-48, for example). In particular, flocculation can be achieved by addition of calcium hydroxide (see col. 2, lines 33-47, for example). The adjustment of particular conventional working conditions (e.g., the the concentration of divalent salt recited in the instant claim 7) is deemed a matter of judicious selection and routine optimization of a result-effective parameter, which is well within the purview of the skilled artisan. Regarding temperature, the broth can be allowed to cool before addition of acid as the final step of flocculation; this temperature can be in the range of 20 to 50 °C. In particular, Kanani et al note that their method is well suited to separating the genus *Bacillus* from its fermentation broth (see col. 1, lines 48-62, for example). Kanani et al note that their method produces large, strong flocs that have a good rate of settling. Their method enables the size of settling tanks and number of centrifuges that are used for separating bacterial flocs in some cases to be reduced (see col. 3, lines 32-50, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to add divalent salt, change the pH of the fermentation broth, and heat the fermentation broth, because Weigel et al teach that *Bacillus* can be induced to

secrete hyaluronic acid into their fermentation broth, and that it is desirable to separate the bacteria from their fermentation broth, and Kanani et al teach a method of producing strong, easily separated flocs by changing pH and temperature of the fermentation broth that allows for the easy purification of hyaluronic acid demanded by Weigel et al.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to employ the flocculation method of Kanani et al in a method of producing and purifying hyaluronic acid taught by Weigel et al.

Response to arguments - 35 USC § 103

Applicants traverse the rejection of claims 1-8 and 12-16 in the Office Action mailed 16 November 2006 under 35 USC 103(a) as being unpatentable over Weigel et al in view of Kanani et al.

Applicants argue that neither Weigel et al nor Kanani et al alone or in combination teach or suggest a method of adding divalent salt as a flocculating agent to the fermentation broth comprising a glycosaminoglycan and a bacillus cell population (Remarks, p. 6, second to last paragraph). Applicants argue that Weigel et al teach that cells can be separated from a fermentation broth by the addition of trichloroacetic acid, not a divalent salt. Applicants also argue that Kanani et al teach a method of flocculation involving raising the pH of the fermentation broth by adding calcium hydroxide, not a method of flocculation involving the addition of a divalent salt.

These arguments have been carefully considered but are not deemed persuasive. The teachings of Weigel et al are highlighted because Weigel et al teach

that production of hyaluronic acid is desirable as it is a useful health product. Production can be achieved by fermenting bacillus bacteria that are capable of producing this glycosaminoglycan, followed by separating the bacteria from the dissolved hyaluronic acid by flocculating them with trichloroacetic acid. All elements are missing except the use of a divalent salt for flocculation.

Kanani et al teach that flocculation of many types of microorganisms, and in particular bacillus bacteria, can be achieved by addition of calcium hydroxide. It is noted that it is well known in the art that bacterial growth requires inclusion of salts in their growth medium. Therefore the process of adding salt to the growth medium and the addition of calcium hydroxide is functionally equivalent to adding divalent salts. Furthermore, Wang DIC et al (Fermentation and Enzyme Technology, John Wiley and Sons, 1979) teaches that it is well known in the art to add calcium chloride and sodium hydroxide to fermentation broths to induce flocculation (see "12.3.1 Whole Cells", p. 257, for example). The functional ingredient for inducing flocculation is, in fact, calcium hydroxide. Therefore Kanani et al have taught a medium competent to induce flocculation comprising all the ingredients instantly claimed as necessary for inducing flocculation, and, as Wang et al would argue, by the same mechanism. Therefore it is deemed to be obvious to one of ordinary skill in the art to include calcium salts and include hydroxide to raise the pH, as required in instant claims 1 and 13.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP
5/9/2007

Jon Weber
Supervisory Patent Examiner